REMARKS

I. Status of the Claims

Claims 21–29 and 31–39 were pending in the application. Upon entry of this amendment, claims 21–26, 28, 29, and 31–39 are pending. Claims 21, 28, 29, 32, 33, 34, 37 and 39 have been amended. Claim 27 has been cancelled. Claims 1–20 and 30 were previously cancelled.

Throughout this response, references made to paragraphs of the specification are made to the paragraph numbering in the publication US2006/0141455.

Claims 21, 32, and 33 have been amended to replace the phrase "DKFZp5661133" with the phrase "DKFZp566I133". Support for these amendments may be found throughout the specification and in particular, at paragraphs [0047]–[0049] and the originally filed claims.

Claim 21 has also been amended to recite that the biological activity is "modulation of a cancerous phenotype." Claim 32 has also been similarly amended to recite that "a difference between the level of DKFZp566I133 expression in the presence and in the absence of the candidate agent modulates a cancerous phenotype." Support for these amendments may be found throughout the specification and in particular, at paragraphs [0059]–[0061] and originally filed claim 27.

Claims 28 and 29 have been amended to depend from claim 21.

Claims 34 and 39 have been amended to clarify antecedent basis.

Claim 37 has been amended to state that the cancerous phenotype is invasiveness. Support for this amendment may be found throughout the specification and in particular, at paragraph [0339].

No new matter has been added, thus entry of the amendments is respectfully requested.

II. Information Disclosure Statement

Applicants acknowledge and thank the Examiner for considering the information disclosure statement and the references cited therein filed August 28, 2009. Applicants acknowledge that only the Abstract of Citation No. 54, WO 93/19191-A1, from the information disclosure filed August 28, 2009 was considered. With respect to Citation No. 37, EP-0345242-A2, Applicants acknowledge that the reference has not been considered and note that in the Response filed January 13, 2010, Applicants stated that Applicants no longer wished to make this reference of record.

Applicants also acknowledge and thank the Examiner for considering the information disclosure statement and the references cited therein filed May 18, 2010.

III. Withdrawn Objections and Rejections

Applicants acknowledge and thank the Examiner for withdrawing the objection to claim 21 for being grammatically incorrect, and for withdrawing the obviousness rejections of claims 21–29 and 31–36.

IV. Priority

The Office has alleged that the disclosure of the prior-filed applications provisional application 60/345,637 and PCT application PCT/US03/00657 fail to provide adequate written description support for the claimed term "DKFZp5661133". In particular, the Office notes that while "DKFZp566I1233" appears throughout these two parent applications, the term "DKFZp56611233" is not supported.

Applicants note that the recitation of "DKFZp56611233" in the claims is a typographical error. Accordingly, the claims have been amended to recite "DKFZp566I1233" rather than "DKFZp56611233". As both provisional application 60/345,637 and PCT application PCT/US03/00657 provide sufficient support for the term "DKFZp566I1233", Applicants respectfully assert that the pending application properly claims the benefit of priority to provisional

application 60/345,637, filed January 8, 2002, and PCT application PCT/US03/00657, filed January 8, 2003.

V. Claim Rejections - 35 USC §112-First Paragraph, New Matter

Claims 21–29 and 31–39 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. In particular, the Office alleges that the term "DKFZp56611233" does not appear to be recited in the pending specification or claims as originally filed.

As noted above, the claims have been amended to correct a typographical error, and now recite "DKFZp566I1233" rather than "DKFZp56611233". Applicants thus respectfully assert that the rejection is now moot, and respectfully request that this basis for rejection be withdrawn.

VI. Claim Rejections - 35 USC §102

Claims 21–26 and 31–35 are rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Publication 2003/0124128 (made of record in the previous Office Action mailed February 17, 2010). In particular, the Office alleges that US 2003/0124128 teaches methods of identifying modulators and a method of screening for modulators (i.e., test compounds or agents) that bind to SEQ ID NO:144, which encodes an amino acid sequence that is 100% identical to DKFZp566I1233.

To the extent the rejection applies to the amended claims, Applicants respectfully traverse the rejection and its supporting remarks. Published U.S. applications are available under §102(e) only if they are an application by another filed in the United States before the invention by the applicant for patent. Further, MPEP § 2136.03 III makes clear that (emphasis added):

> The 35 U.S.C. 102(e) critical reference date of a U.S. patent or U.S. application publications and certain international application publications entitled to the benefit of the filing date of a provisional application under 35 U.S.C. 119(e) is the filing date of the provisional application with certain exceptions if the provisional application(s) properly supports the

subject matter relied upon to make the rejection in compliance with 35 U.S.C. 112, first paragraph.

Applicants respectfully assert that US 2003/0124128 is not available as §102(e) prior art, as its critical reference date does not pre-date the January 8, 2002 priority date of the instant application. US 2003/0124128 was published July 3, 2003 and claims priority to six provisional applications: 60/299,887 filed June 21, 2001; 60/301,572 filed June 27, 2001; 60/306,501 filed July 18, 2001; 60/325,002 filed September 25, 2001; 60/362,585 filed March 5, 2002; and 60/380,391 filed May 14, 2002. Applicants respectfully point out that the gene corresponding to DKFZp566I1233 (i.e., SEQ ID NO: 144), the subject matter which forms the basis of the pending rejection, was first disclosed in the provisional application 60/362,585, filed March 5, 2002. As the four provisional applications filed prior to March 5, 2002 do not disclose the gene corresponding to DKFZp566I1233, they do not properly support the DKFZp566I1233 subject matter in compliance with 35 U.S.C. § 112, first paragraph. Accordingly, at best, the §102(e) critical reference date for US 2003/0124128 is March 5, 2002.

As the priority date of the instant application, January 8, 2002, pre-dates the §102(e) critical reference date of US 2003/0124128, this patent application is not available as §102(e) art. Applicants thus request that this basis for rejection be withdrawn.

VII. Claim Rejections - 35 USC §103

Claims 21–29, 31–34, and 37–39

Claims 21–29, 31–34, and 37–39 are rejected under 35 § U.S.C. 103(a) as being unpatentable over WO 01/60860 A2 ('860) (made of record in the previous Office Action mailed February 17, 2010) in view of WO 01/12662 A2 ('662) (made of record in the previous Office Action mailed February 17, 2010). In particular, the Office alleges that it would have been obvious for one of skill in the art, at the time the invention was made, to combine the teachings of the '860 and '662 patent applications to devise the claimed methods, as both references taught that the

DKFZp566I133 gene is associated with cancer and taught that methods for identifying an anti-cancer agent were well known in the art.

To the extent the rejection applies to the amended claims, Applicants respectfully traverse the rejection and its supporting remarks. The Office has failed to establish a *prima facie* case of obviousness, as one of skill in the art would have no reason to modify or combine the references to produce the claimed invention.

As amended, independent claim 21 is directed to a method for identifying a cancer therapeutic agent that modulates a biological activity of a gene product differentially expressed in a cancerous cell as compared to a normal cell, wherein the biological activity is modulation of a cancerous phenotype. Additionally, as amended, independent claim 32 is directed to a method of screening a candidate agent to identify a cancer therapeutic by contacting a cell that expresses DKFZp566I133 with a candidate agent, and detecting a difference between the level of expression of DKFZp566I133 in the presence and absence of the candidate agent, wherein a difference between the level of DKFZp566I133 expression in the presence and in the absence of the candidate agent modulates a cancerous phenotype and indicates that the candidate agent is a cancer therapeutic. Support for such claims is found, for example, in sections of the instant application demonstrating that DKFZp566I133 is differentially expressed in cancer cells, and that modulation of DKFZp566I133 in cancer cells modulates cancerous phenotypes (see Examples 7, 9 and 10).

Applicants respectfully submit that the '860 application does not teach or suggest the presently claimed methods of identifying or screening for a cancer therapeutic that modulates a cancerous phenotype by modulating the biological activity or level of expression of DKFZ p566I133 differentially expressed in a cancerous cell, as the reference does not disclose that DKFZ p566I133 is differentially expressed in cancer cells. The Office alleges that the '860 application teaches SEQ ID NO: 29252 (i.e., DKFZ p566I133) among several thousands of genes that are differentially expressed in prostate cancer cells. However, the reference does not disclose SEQ ID

NO: 29252 as such a gene. The '860 application makes clear that the disclosed genes associated with prostate cancer are listed in Tables 1–9 (see page 15, lines 8–10):

> The polynucleotides set forth in Tables 1-9 represent previously unidentified nucleotide sequences. These nucleotide sequences were identified through subtracted library experiments described herein.

SEQ ID NO: 29252 is not found in Tables 1–9 of the '860 application.

With regard to the contents of Tables 1-9, the '860 application states that Tables 1 and 3 disclose SEQ ID NOs: 1–5846 (see page 94, line 14), Tables 2 and 4 disclose SEQ ID NOs: 1–3323(see page 95, line 12), Table 5 discloses SEQ ID NOs: 5847–10246 (see page 95, line 25), Table 6 discloses the sequences of Tables 1–4 (see page 98, line 10), Table 7 discloses the sequences of Tables 1 and 2 with vector sequences removed (see page 98, lines 6–7), Table 8 discloses SEQ ID NOs: 10247–22286 (see page 96, line 9), and Table 9 discloses SEQ ID NOs: 22287–22548 (see page 97, line 2). The '860 application thus fails to indicate that Tables 1–9 disclose genes with sequence identifiers greater that SEQ ID NO: 22548, much less SEQ ID NO: 29252.

As the '860 application does not teach that SEQ ID NO: 29252 was identified in the results of the subtracted library experiments presented in Tables 1–9, the reference fails to teach or suggest that SEQ ID NO: 29252 (i.e., DKFZ p566I133) is differentially expressed in cancer cells. Without such a teaching, one of skill in the art would have had no reason to modify the teachings of the '860 application to devise the presently claimed methods of identifying or screening for a cancer therapeutic that modulates a cancerous phenotype by modulating the biological activity or level of expression of DKFZp566I133 differentially expressed in a cancer cell.

This deficiency in the '860 application cannot be remedied by the '662 application, as this reference also fails to teach or suggest that DKFZp566I133 (i.e., SEQ ID NO: 54) is differentially expressed in cancer cells, and fails to teach that modulating the activity or level of expression of DKFZp566I133 affects a cancerous phenotype.

The '662 application relates to human membrane associated proteins that were identified from cDNA libraries constructed from RNA isolated from various human tissues, including diseased and cancerous tissues (see page 23, line 33 through page 24, line 35 and Tables 1–4). The proteins were identified by isolating cDNA clones from the libraries, sequencing the clones, and analyzing the sequences with sequence alignment software to identify human membrane associated proteins (see Examples I through III). As noted by the Office, one such identified protein is SEQ ID NO: 54 (i.e., DKFZ p566I133), which was identified from RNA isolated from a squamous cell carcinoma tumor sample (see the section of Table 4 on page 98). However, expression levels of SEQ ID NO: 54 in a cancer cell were not compared to expression levels of SEQ ID NO: 54 in a normal cell. As such, the '662 application fails to teach or suggest that SEQ ID NO: 54 is differentially expressed in a cancer cell.

Moreover, despite the Office's allegation that the '662 application teaches methods of identifying or screening for an anti-cancer agent that modulates the activity or expression of DKFZp566I133, the'662 application does not provide a specific teaching that modulating the activity or level of expression of SEQ ID NO: 54 affects a cancerous phenotype, such as cell proliferation or anchorage-independent growth. Nor does the '662 application provide any examples of agents that modulate a cancerous phenotype by modulating the activity or expression of SEQ ID NO: 54. By contrast, the instant application provides specific examples of agents that modulate the cancerous phenotype of cancer cells, including cell proliferation and anchorage-independent growth, by modulating the expression of DKFZp566I133 (see Examples 9 and 10).

With respect to the Office's allegation that the '662 application teaches methods for screening a compound for effectiveness in altering expression of DKFZp566I133 in breast cancer cells, Applicants respectfully point out that the '662 application does not teach or suggest that DKFZp566I133 is expressed in breast cancer cells. Rather, the '662 application teaches that SEQ ID NO: 54 (i.e., DKFZp566I133) was identified from a squamous cell carcinoma tumor sample (see the section of Table 4 on page 98).

Given that the '662 application fails to teach or suggest that DKFZp566I133 is differentially expressed in cancer cells and that modulating the activity or level of expression of DKFZp566I133 affects a cancerous phenotype, one of skill in the art would have had no reason to combine or modify the teachings of the '662 application with the teachings of the '860 application to produce the currently claimed invention.

For at least the reasons set forth above, the Office has failed to establish a *prima facie* case of obviousness for claims 21, 32, and all dependent claims therefrom. Applicants thus respectfully request that this basis for rejection be withdrawn.

Claims 35 and 36

Claims 35 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 01/60860 A2 ('860) in view of WO 01/12662 A2 ('662) as applied to claims 21-29, 31-34, and 37-39, and further in view of U.S. Patent No. 6,844,325 ('325) (of record).

To the extent the rejection applies to the amended claims, Applicants respectfully traverse the rejection and its supporting remarks. The Office has failed to establish a *prima facie* case of obviousness, as one of skill in the art would have had no reason to combine the references to produce the claimed invention.

As discussed above, the '860 and '662 applications fail to teach or suggest that DKFZp566I133 is differentially expressed in cancer cells and that modulating the activity or level of expression of DKFZp566I133 affects a cancerous phenotype. The '325 patent fails to remedy the deficiencies of the '860 and '662 applications. The '325 patent relates primarily to various clones over-expressed in breast cancer tumor tissue, none of which include DKFZp566I133. The '325 patent thus fails to teach methods of identifying or screening for a cancer therapeutic that modulates a cancerous phenotype by modulating the biological activity or level of expression of DKFZp566I133 differentially expressed in a cancerous cell.

For at least the reasons set forth above, the Office has failed to establish a *prima facie* case for obviousness of claims 35 and 36. Applicants thus respectfully request that this basis for rejection be withdrawn.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark Office determines that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing **Docket No. 636092105200**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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